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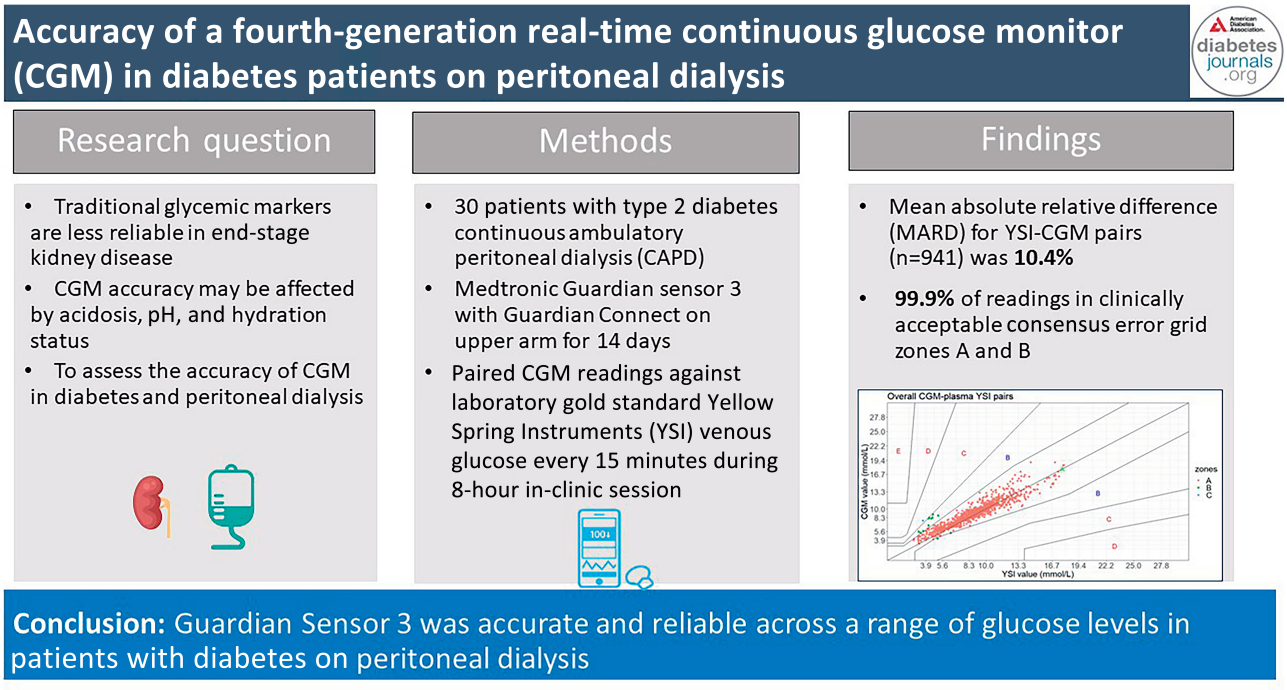

ARTICLE HIGHLIGHTS

- Alternative glycemic markers are needed as HbA_{1c} is less reliable in end-stage kidney disease. Few studies have evaluated accuracy of continuous glucose monitor (CGM) sensors in peritoneal dialysis, which are increasing in popularity.
- Thirty patients with type 2 diabetes on continuous ambulatory peritoneal dialysis wore a Medtronic Guardian Sensor 3. CGM readings were compared against Yellow Springs Instrument venous glucose during an 8-h in-clinic session.
- The mean absolute relative difference was 10.4% from 941 matched pairs, and 99.9% of the readings were within clinically acceptable consensus error grid zones A and B.
- We showed satisfactory performance of a real-time CGM sensor, supporting future use in peritoneal dialysis populations.

Evaluation of a Fourth-Generation Subcutaneous Real-Time Continuous Glucose Monitor (CGM) in Individuals With Diabetes on Peritoneal Dialysis

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BRIEF REPORT

OBJECTIVE

To evaluate the performance of a real-time continuous glucose monitor (CGM) in individuals with diabetes on peritoneal dialysis (PD).

RESEARCH DESIGN AND METHODS

Thirty participants with type 2 diabetes on continuous ambulatory PD wore a Guardian Sensor 3 on the upper arm paired with Guardian Connect for 14 days. We compared CGM readings against Yellow Springs Instrument (YSI) venous glucose during an 8-h in-clinic session with glucose challenge.

RESULTS

The mean absolute relative difference (MARD) was 10.4% (95% CI 9.6, 11.7) from 941 CGM-YSI matched pairs; 81.3% of readings were within %15/15 of YSI values in the full glycemic range. Consensus error grid analysis showed 99.9% of sensor values in zones A and B. There were no correlations between pH, uremia, hydration status, and MARD.

CONCLUSIONS

We showed satisfactory performance of a real-time CGM sensor in PD patients with diabetes, supporting future use to facilitate treatment decisions.

Diabetic kidney disease is the leading cause of end-stage kidney disease (ESKD) worldwide (1). Given the growing demand for renal placement therapy, peritoneal dialysis (PD) is increasingly favored as a home-based and cost-effective option rather than hemodialysis (HD) (2). Peritoneal glucose exposure, especially hypertonic glucose solutions, induce greater interstitial glucose surge and glycemic variability (3). The accuracy of traditional glycemic markers (e.g., glycated hemoglobin [HbA_{1c}]) is affected by use of iron and erythropoietin-stimulating agents (4). The latest Kidney Disease Improving Global Outcomes (KDIGO) guideline advocates the use of periodic continuous glucose monitoring (CGM) alongside HbA_{1c} in stage 4 to 5 chronic kidney disease (5). Recently published studies focused on the evaluation of accuracy of CGM in HD patients (6–8). However, few studies have been conducted in PD patients

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(9,10), mostly using self-monitoring of blood glucose (SMBG) as the comparator within a limited glycemic range.

In this study, we evaluated the performance of the real-time fourth-generation Medtronic Guardian Sensor 3 CGM against a laboratory gold standard reference (Yellow Spring Instrument [YSI] glucose analyzer) in patients undergoing continuous ambulatory PD (CAPD). We additionally explored renal-specific factors that might influence its accuracy, including uremia, acidosis, and fluid status.

RESEARCH DESIGN AND METHODS

This was a single-center, prospective, open-label study of Guardian Connect with Guardian Sensor 3 in 30 participants with diabetes on CAPD, at the Prince of Wales Hospital, Hong Kong Special Administrative Region, which received ethical approval (CREC-2020.365, NCT04776811). Participants were diagnosed with type 1 or type 2 diabetes for at least 3 months, on CAPD for at least 3 months, and aged 18–75 years old; participants were excluded if they had HbA_{1c} >11%, peritonitis in the previous month or were on icodextrin PD solutions (Supplementary Methods).

Fasting plasma glucose, complete blood count, hematocrit, liver and renal function tests, and HbA_{1c} were collected at screening. Dialysis adequacy was represented by total urea clearance adjusted by the volume of distribution of urea (total Kt/V), which was the sum of renal and peritoneal urea clearance (peritoneal Kt/V) respectively. On day 1, one Guardian Sensor 3 was inserted on the upper arm and paired with the Guardian Connect app (Apple iPhone XR) and calibrated at least 12 h using a Contour Plus (Ascensia Diabetes Care, Switzerland) glucometer. Volume status was determined by a bioimpedance spectroscopy device (Body Composition Monitor, Fresenius Medical Care, Germany) (11).

Participants were randomly allocated to a single 8-h in-clinic measurement on day 3 or day 5 in a 1:1 ratio. Venous blood (1 mL) was sampled from an intravenous cannula and whole blood glucose measured on the YSI 2300 STAT glucose analyzer (Yellow Springs Instruments, Yellow Springs, OH) every 15–20 min for 8 h (33 time points per subject). Capillary blood glucose was measured hourly. Blood glucose was deliberately manipulated via carbohydrate consumption and insulin dosing with rapid-acting insulin lispro (Humalog, Eli Lilly, Indianapolis, IN) to achieve YSI sample measurements within target glucose ranges between 60 and 350 mg/dL following a protocol-specific guideline. Timing of CAPD exchanges, meals, and insulin doses were recorded. Serum fructosamine, pH, and urea were measured. For the remaining time, participants used the Guardian Connect system at home for up to 14 days, with sensor replacement on day 7 ± 1 in the upper arm. User satisfaction on Guardian Connect with Guardian Sensor 3 was evaluated using an 11-item questionnaire (Supplementary Fig. 1).

The primary outcome was mean absolute relative difference (MARD) between CGM-plasma YSI glucose pairs during the in-clinic session. This was estimated across the full glycemic range and stratified by glucose ranges. Secondary outcomes included clinical accuracy by consensus error grid analysis and agreement using the %15/15, %20/20 criteria. MARD and agreement were evaluated for in-clinic CGM-SMBG pairs. We analyzed accuracy at different rates of change (RoC) of plasma YSI glucose. A true hypoglycemic detection was considered if at least one CGM value was below the threshold within 15 min of a hypoglycemic event (defined as a plasma YSI

Table 1—Participant characteristics

Variable	Data value (*N* = 30)
Age (years)	64.7 ± 5.6
Sex	
Male	23 (76.7)
Female	7 (23.3)
BMI (kg/m^2)	25.4 ± 3.9
Weight (kg)	66.3 ± 13.6
Type 2 diabetes	30 (100)
Diabetes duration (years)	17.6 ± 8.0
CAPD duration (months)	16.2 ± 19.5
On dextrose 1.5% PD solution only	22 (73)
At least one bag of hypertonic PD solution (defined as dextrose concentration ≥2.3%)	8 (27)
On insulin	19 (66.7)
On dipeptidyl peptidase 4 inhibitors	14 (46.7)
Total Kt/V	2.3 ± 0.66
Peritoneal Kt/V	1.2 ± 0.30
Dialysate-to-plasma creatinine ratio at 4 h	0.65 ± 0.14
Daily peritoneal glucose exposure (g/day)	96.0 ± 16.2
HbA_{1c} (%)	7.1 ± 0.9
HbA_{1c} (mmol/mol)	53.9 ± 10.4
Fasting plasma glucose (mmol/L)	8.1 ± 3.0
Albumin (g/L)	29.8 ± 3.5
Fructosamine (μmol/L)	275 ± 54.0
Albumin-adjusted fructosamine (μmol/g)	929 ± 198
Plasma creatinine (μmol/L)	673 ± 189
Hemoglobin (g/dL)	10.7 ± 1.3
Hematocrit (%)	32.2 ± 4.1
Urea (mmol/L)	23.1 ± 5.8
pH	7.39 ± 0.033
Volume of overhydration (L)	3.01 ± 1.61

Data are presented as mean ± SD or *n* (%).

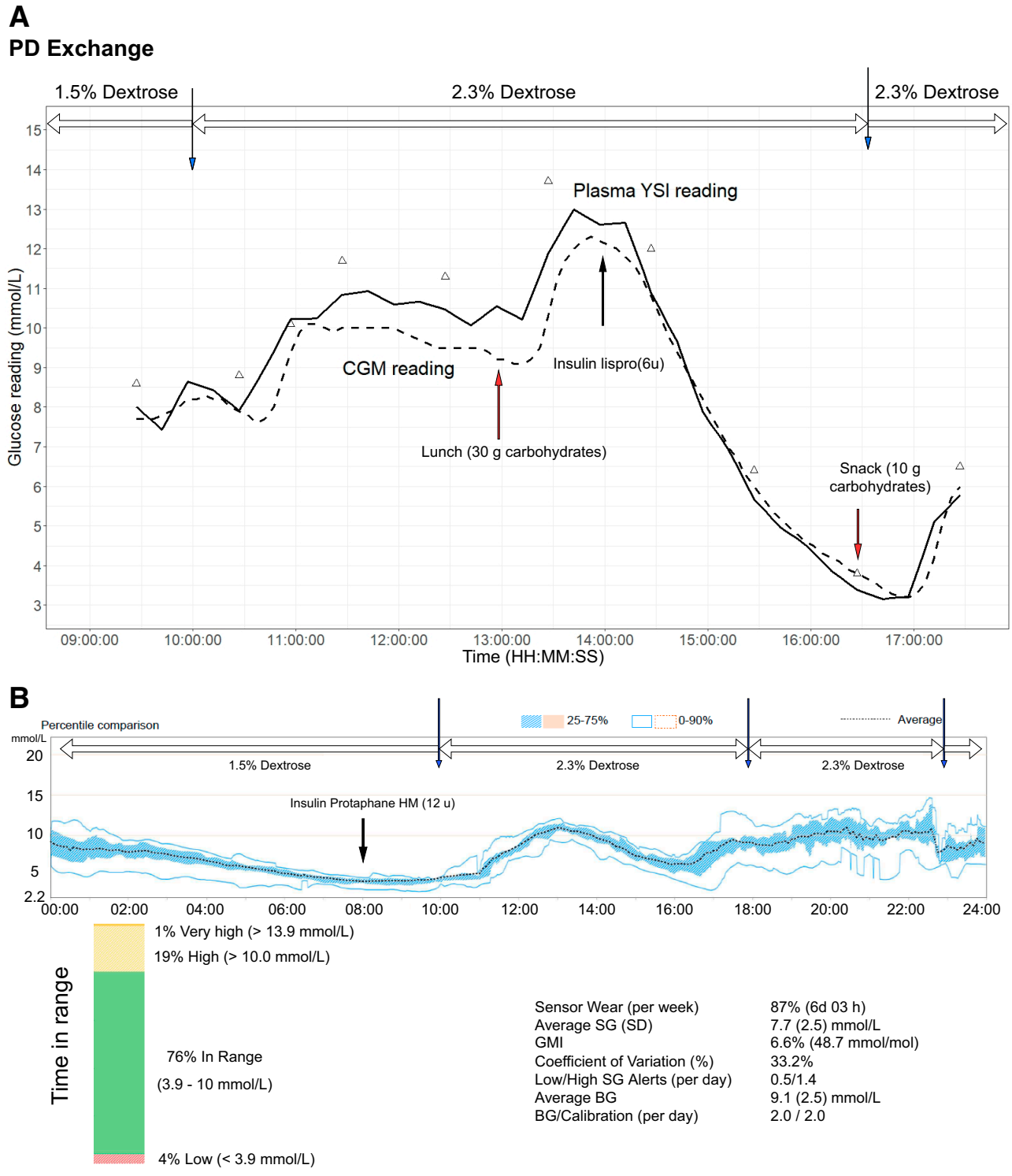

Figure 1—Example glucose profile illustrating the meal, insulin, PD exchange times, and doses during the 8-h in-clinic visit (*A*) and 14-day ambulatory glucose profile of the same patient (*B*). The patient was a 63-year-old woman, with HbA_{1c} 7.4%, and on Protaphane HM 12 units prebreakfast on a three-bag PD regimen of 2.3%, 2.3%, and 1.5% dextrose, with exchanges at 1000, 1800, and 2300 h. *A*: YSI plasma glucose is shown in the solid line, CGM values are shown in the dotted line, and triangles are SMBG values. The maximum YSI glucose was 13.0 mmol/L at 1340 h and lowest was 3.2 mmol/L at 1640 h. An additional 6 units insulin lispro was given during the glucose challenge. *B*: The 14-day ambulatory glucose profile demonstrates asymptomatic hypoglycemia at 0700–0800 (4% time below range) and also hyperglycemic excursion peaking ∼2 h after hypertonic PD exchange. The patient was subsequently switched to insulin glargine to prevent hypoglycemia.

glucose of ≤3.9 mmol/L). A true hyperglycemic detection was considered as at least one CGM value above threshold within 15 min of a hyperglycemic event (defined as a plasma YSI glucose ≥10.0 mmol/L). A true hypoglycemic alarm was considered if the CGM alert was accompanied by at least one YSI value ≤3.9 mmol/L within a 15-min window. A true hyperglycemic alarm

Table 2—Percent agreement and MARD/MAD between CGM-YSI plasma glucose pairs across glycemic ranges

	Paired CGM-plasma YSI readings (*n*)	% (95% CI)	%15/15 (%, lower 95% CI)	%20/20 (%, lower 95% CI)	%30/30 (%, lower 95% CI)	%40/40 (%, lower 95% CI)
MARD						
Overall	941	10.4 (9.6, 11.2)	81.3 (78.8)	88.6 (86.6)	96.9 (95.8)	98.8 (98.1)
Euglycemic range (3.9–10 mmol/L)	600	10.7 (9.7, 11.7)	79.5 (76.3)	88 (85.4)	96.2 (94.6)	98.5 (97.5)
Hyperglycemic range (>10 mmol/L)	311	7.4 (6.9, 8.1)	88.7 (85.2)	93.9 (91.2)	99.7 (99.0)	100 (100)
MAD mmol/L (95% CI)						
Hypoglycemic range (<3.9 mmol/L)	30	1.2 (0.86, 1.5)	40 (21.4)	46.7 (27.7)	83.3 (69.2)	93.3 (83.9)

was considered if at least one YSI value was above the threshold ≥10 mmol/L within 15 min of the alarm. Correlations between MARD, pH, urea, and hydration parameters were determined by Pearson correlation. Data were analyzed using R 4.1.2 software (R Core Team, 2021) (Supplementary Methods).

Data and Resource Availability

Deidentified data are available from the corresponding author upon reasonable written request.

RESULTS

There were 30 participants enrolled between 8 March 2021 and 15 August 2022, and 29 completed the in-clinic session (day 3, *n* = 14; day 5, *n* = 15). One participant was withdrawn prior to the YSI session due to repeated sensor failure. A total of 961 pairs of CGM-plasma YSI and 259 pairs of CGM-SMBG values were collected. The average age was 64.7 ± 5.6 years, 77% were men, diabetes duration was 17.6 ± 8.0 years, HbA_{1c} was 7.1 ± 0.9%, and CAPD duration was 16.2 ± 19.5 months. All used glucose-containing PD fluids, with eight on hypertonic solutions (at least one exchanges with dextrose concentration >1.5%) (Table 1). Twenty-six participants completed 14-day sensor wear. Of those with >70% valid CGM data (*n* = 22), time-in-range (TIR; 3.9–10.0 mmol/L) was 68.1 ± 20.1%, time >10.0 mmol/L was 31.2 ± 20.8%, and time <3.9 mmol/L was 0.7 ± 1.3%. Mean glucose management indicator was 7.2 ± 0.6%, and the coefficient of variation was 26.4 ± 7.1%. Correlations between HbA_{1c} -glucose management indicator (r = 0.47) and TIR-fructosamine (r = −0.34) were moderate. Example glucose profiles during in-clinic and home use are shown in Fig. 1.

Overall, MARD of CGM-plasma YSI pairs was 10.4% (95% CI 9.6, 11.2). The agreement rates by %15/15, %20/20 criteria were 81.3% (lower 95% CI 78.8) and 88.6% (86.6), respectively. In hypoglycemic range <3.9 mmol/L, mean absolute difference (MAD) of CGM-plasma YSI pairs was 1.2 mmol/L (95% CI 0.86, 1.5) or 21.6 mg/dL (95% CI 16, 27) (Table 2). In the full glycemic range, the percentage of CGM-YSI pairs in zone A was 98.5% (*n* = 927) and in zone B was 1.4% (*n* = 13) of the consensus error grid (Fig. 2). In hypoglycemia, 96.7% of CGM-plasma YSI pairs were in zones A and B. The MARD for CGM-SMBG pairs was 9.3% (95% CI 8.3, 10.3) (Supplementary Table 1). The MARD was 10.7% (9.7, 11.7) at a negative RoC and 9.1% (95% CI 8.0, 10.1) at a positive RoC (Supplementary Table 2). The correct detection rates for hyperglycemic events were 96.5% (301 of 312 events) and 60% for hypoglycemic events. The true alarm rate for hyperglycemic alarm was 94.9% (*n* = 334) and was 100% (six of six events) for hypoglycemic alarms (Supplementary Table 3).

No significant correlations were observed between MARD of CGM-plasma YSI pairs with pH level, plasma urea, extracellular water volume, and relative hydration index. (Supplementary Table 4). Mild bruising occurred at the sensor site in two patients and discomfort at the sensor site in one patient, which led to premature termination on day 9. There were four other nonsevere adverse events unrelated to the device. Overall user satisfaction was high (Supplementary Table 5).

CONCLUSIONS

To our knowledge, this was the first study that evaluated the accuracy and performance of a contemporary real-time CGM device in PD patients with diabetes. Our study showed that the Medtronic Guardian Sensor 3 was accurate, with an overall MARD of 10.4%. Consensus error grid analysis revealed that nearly all (99.9%)

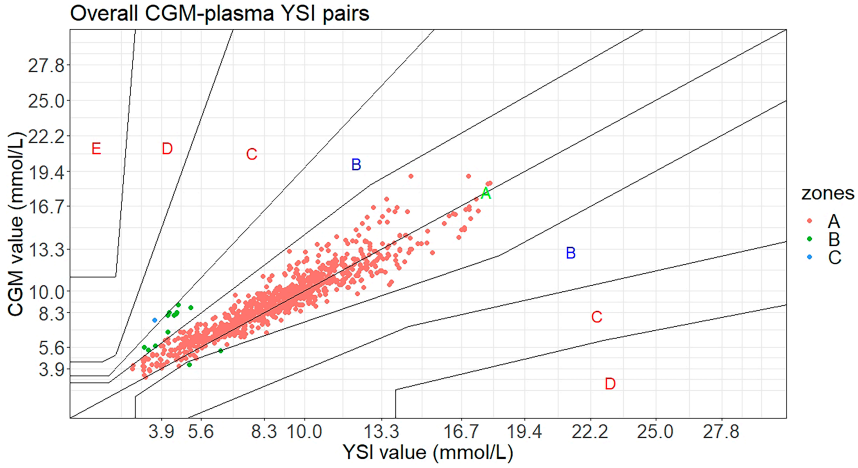

Figure 2—Consensus error grid analysis of glucose values of Medtronic Guardian Sensor 3 vs. YSI plasma glucose values in the full glycemic range (pooled data for 30 patients with 941 YSI-CGM pairs).

CGM-YSI pairs fell into zone A+B. Importantly, the accuracy of the sensor was not influenced by acidosis, urea concentration, and volume overload.

The Medtronic Guardian Sensor 3 provided accurate glucose readings in patients with type 1 or 2 diabetes without ESKD (MARD 9.1 ± 8.34% on the arm) using YSI as a reference (12), which was comparable to our results in PD. In other studies, the overall MARD was 13.8% compared with SMBG (n = 684) when a factory-calibrated CGM (Dexcom G6-Pro) was evaluated in 20 HD patients (6). Similarly, in a multicenter study in Japan, FreeStyle Libre was significantly lower than capillary glucose, with MARD of 23.4% in HD (7). Direct comparisons between dialysis modalities may be difficult given significant glucose fluctuations in the intradialytic milieu during HD (13). Limited available evidence in patients on PD revealed that MARD of CGM was ∼15–20% (9,10). Nonetheless, most, if not all, of the previous studies used SMBG as a reference standard, in contrast to YSI in our study. Calibration requirements and sensor sites may also explain differences between our results and prior reports.

Our major strength is use of YSI as the gold standard reference for assessment of CGM accuracy. We captured a wide range of glucose levels with diet/insulin manipulation while maintaining the patients' usual PD regimen to mimic real life. Moreover, we examined several renal-specific factors, such as volume status by bioimpedance, on sensor performance.

Our study had a few limitations. First, the sample size was relatively small compared with sensor evaluation studies for regulatory approval. Nevertheless, the number of matched pairs (941 CGM-YSI pairs) was larger than most studies on dialysis (6,8,14). We captured a limited number of CGM-YSI data pairs (3.4%) in hypoglycemic range due to ethical and safety concerns. In this study, the correct hypoglycemic detection rate was 60%, and patients should perform confirmatory SMBG where sensor glucose does not match with symptoms, bearing in mind the Guardian Sensor is only approved for adjunctive use. We did not perform head-to-head comparisons versus other sensors or against an age- or sex-matched non-ESKD control group. Lastly, patients on icodextrin were excluded due to possible sensor interference with icodextrin metabolites.

In conclusion, we showed the Medtronic Guardian Sensor 3 was accurate and reliable across a wide range of glucose levels in PD patients with diabetes. Real-time CGM may facilitate detection of asymptomatic glucose excursions related to hypertonic exchanges (15). Future studies will investigate whether optimization of CGM-based metrics will improve clinical outcomes in PD.

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Author Contributions. J.K.C.N., J.L., and E.C. contributed to conception of the article, data collection, statistical analysis, interpretation of results, and drafting, revision, and approval of the manuscript. A.O.Y.L., E.S.H.L., R.C.W.M., P.K.T.L., C.C.S., and J.C.N.C. contributed to data analysis and interpretation of results, critically revised the manuscript, and approved the final version. E.C. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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